REMARKS

Claim Amendments

Applicant has canceled claims 4 and 8, without prejudice.

Applicant has amended claim 1 to delete the expression "or a derivative thereof."

Applicant has amended claim 2 to recite a method comprising the reaction of solasodine with tetra-O-benzoyl-α-D-glucopyranosyl bromide, tetra-O-acetyl-α-D-glucopyranosyl bromide or tetra-O-pivaloyl-α-D-glucopyranosyl bromide. Support for this amendment may be found, *inter alia*, in claim 4, as originally filed. Applicant has also deleted the term "as defined in claim 1". As the Examiner noted in the Advisory Action, the method of claim 2 does not produce the conjugates of claim 1.

Applicant has amended claim 3 to recite a method comprising the glycosylation of the diol of formula IIa with tri-O-benzoyl-α-L-rhamnopyranosyl bromide or tri-O-pivaloyl-α-L-rhamnopyranosyl trichloroacetimidate. Support for this amendment may be found, *inter alia*, in claim 8, as originally filed. Applicant has also corrected claim 2 to recite R_2 not R_3, to recite "pivaloyl" not "acetyl" (as required by the above amendment) and to delete the reference to claim 1.

Applicant makes these amendments expressly without waiver of their right to file for and to obtain claims directed to the canceled or amended subject matter in applications claiming priority and benefit herefrom.

None of these amendments constitutes new matter. They place the recitations of dependent claims 4 and 8 into the independent claims. They also make the claims consistent with those amendments. Finally, the amendments respond to and overcome the specific

rejections made in the Final Office Action and in the Advisory Action. Their entry is requested. Upon entry of the amendments, claims 1-3, 5-7, and 9 will be pending in this application.

Obviousness-Type Double Patenting

Claims 1-9 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over co-pending United States patent application 10/555,038 in view of Cham et al. (U.S. Patent 5,958,770) ("***Cham***)" and Schmidt et al. (U.S. Patent 6,242,583) ("***Schmidt***"). Applicant has canceled claims 4 and 8. Applicant requests that the remainder of this rejection be held in abeyance until allowable subject matter is found in the instant application and the '038 application. Applicant will then respond to the obviousness-type double patenting rejection in the appropriate way, *i.e.*, by argument or the filing of the appropriate Terminal Disclaimer.

Rejection under 35 U.S.C. § 102(b)

Claim 1 stands rejected under 35 U.S.C. § 102(b) as allegedly anticipated by ***Cham*** (U.S. patent 5,958,770) The Examiner acknowledges that ***Cham*** does not refer to glucose-solasodine conjugates wherein the glucose moiety is substituted by a benzoyl or a pivaloyl group. However, the Examiner contends that claim 1 is not limited to glucose-solasodine conjugates substituted by a benzoyl or a pivaloyl group, but also encompasses derivatives such as those allegedly referred to by ***Cham***.

Without conceding the correctness of this rejection, Applicants have amended claim 1 to delete the expression "or a derivative thereof." Amended claim 1 refers only to a glucose-solasodine conjugate wherein the glucose moiety is substituted by a benzoyl or a

pivaloyl group. Accordingly, claim 1 is not anticipated by ***Cham***. Indeed, in the Advisory Action, the Examiner withdrew this novelty rejection in light of amended claim 1.

Rejections under 35 U.S.C. § 103(a)

Claim 1 stands rejected under 35 U.S.C. § 103(a) as allegedly obvious over ***Cham*** in view of ***Schmidt*** (U.S. patent 6,242,583) The Examiner contends that ***Cham*** refers to glucose conjugates of solasodine wherein the hydroxyl groups may be substituted by acetyl groups, and that ***Schmidt*** teaches the conventional use of acetyl, benzoyl, and pivaloyl groups in sugar synthesis. The Examiner concludes that the skilled artisan at the time the invention was made would have been motivated to substitute a benzoyl or pivaloyl group for the acetyl group in a compound referred to in ***Cham*** to produce a compound of the claimed invention. Applicant traverses.

Cham refers to solasonine or solamargine derivatives that play a role ***in control of cellular function***. ***Cham*** does not refer to glucose-solasodine conjugates that are advanced intermediates in solamargine or solasonine synthesis. The advanced intermediates of the claimed invention are not synthesized or selected based on their ability to control cellular function. One skilled in the art would, therefore, not expect that a compound referred to in ***Cham*** would be useful in solamargine or solasonine synthesis. The skilled worker would thus have had no reason to substitute a benzoyl or pivaloyl group for the acetyl group in the compounds allegedly referred to in ***Cham*** to produce a compound of the claimed invention. The skilled worker would also have no reason to believe that such substitution would be advantageous in solamargine or solasonine synthesis. Accordingly, claim 1 is not obvious over ***Cham*** in view of ***Schmidt***.

Claim 1 is a compound claim. The rejection of that claim over ***Cham*** in view of ***Schmidt*** is illogic. It cannot be that the recitation of a first compound having a specific substituent, here acetyl, makes obvious a second compound with different substituents, here benzoyl and pivaloyl, because a third compound, not even in the same class as the first compound, happens to have the other substituents. Were that the rule, virtually all chemical compounds would be obvious. Plainly, they are not. For the same reasons, amended claim 1 is not obvious over ***Cham*** in view of ***Schmidt***.

Claims 2 and 4-7 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over ***Cham*** in view of Holick (U.S. Patent 5,612,317) ("***Holick***") and ***Schmidt***. The Examiner acknowledges that ***Cham*** does not disclose a process for preparing glucose conjugates of solasodine by reacting solasodine with a protected glucopyranosyl donor. However, the Examiner contends that ***Holick*** refers to a method for glycosylating an analogous steroid derivative by reacting the steroid with a protected sugar donor. The Examiner further contends that ***Schmidt*** refers to the use of acetyl, benzoyl, and pivaloyl protecting groups in sugar synthesis. The Examiner concludes that one of ordinary skill at the time the invention was made would have been motivated to use the method allegedly referred to in ***Holick*** and the protecting groups allegedly referred to in ***Schmidt*** to prepare the compounds allegedly referred to in ***Cham***. Applicant traverses.

As described above, the compounds of the claimed invention are ***not*** obvious over ***Cham*** in view of ***Schmidt***. ***Holick*** does not overcome the deficiencies of ***Cham*** and ***Schmidt*** in rendering obvious a compound or method of the claimed invention. However, without conceding the correctness of this rejection, Applicants have canceled claim 4 and amended claim

2 to recite the reaction of solasodine with tetra-O-benzoyl-α-D-glucopyranosyl bromide, tetra-O-acetyl-α-D-glucopyranosyl bromide or tetra-O-pivaloyl-α-D-glucopyranosyl bromide. ***Cham***, ***Holick***, and ***Schmidt*** do not refer to these specific D-glucopyranosyl donors. Accordingly, claim 2 and claims 5-7 depending therefrom are not obvious over ***Cham*** in view of ***Holick*** and ***Schmidt***.

Claims 3, 8 and 9 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over ***Cham*** in view of Ohira et al. (U.S. Patent 6,084,081) ("***Ohira***"). The Examiner states that ***Cham*** refers to solamargine and glucose-solasodine conjugates and that glycosylation of a sugar moiety was well known in the art, as referred to by ***Ohira***, at the time the invention was made. The Examiner concludes that the skilled artisan at the time the invention was made would have been motivated to use a method of glycosylation of a sugar moiety, as referred to by ***Ohira***, to glycosylate a glucose-solasodine conjugate, as referred to by ***Cham***, to prepare solamargine, as referred to by ***Cham***. Applicant traverses.

As described above, the compounds of the claimed invention are ***not*** obvious over ***Cham***, which allegedly refers to compounds that play a role in ***control of cellular function*** and does not refer to glucose-solasodine conjugates that are advanced intermediates in solamargine or solasonine synthesis. ***Ohira*** does not overcome the deficiencies of ***Cham*** in rendering obvious the methods of the claimed invention. However, without conceding the correctness of this rejection, Applicants have canceled claim 8 and amended claim 3 to recite the specific α-L-rhamnopyranosyl donors tri-O-benzoyl-α-L-rhamnopyranosyl bromide or tri-O-pivaloyl-α-L-rhamnopyranosyl trichloroacetimidate. Neither ***Cham*** nor ***Ohira*** refers to these α-L-

rhamnopyranosyl donors. Accordingly, claim 3 and claim 9 depending therefrom are not obvious over ***Cham*** in view of ***Ohira***.

In the Advisory Action, the Examiner has maintained her rejection of the claims as obvious over ***Cham*** in combination with the other cited documents. Applicant requests reconsideration.

As explained above, ***Cham*** fails as a primary document because it provides no teaching or suggestion that its compounds are or would be useful as intermediates in solamargine or solasonine synthesis. Without that teaching, the general synthetic methods or protective groups of the other documents are not relevant. Indeed, the Examiner has pointed to nothing in the skill of the art or conditions in the market place that would have suggested the claimed intermediates and methods to the skilled worker.

In her Advisory Action, The Examiner points to ***Cham's*** recitation of a large number of glycoalkaloids, including some substituted with glucose, and its recitation that solasodine glycosides can be isolated as a mixture of solamargine and solasonine or as separate components to find the missing teaching, discussed above in ***Cham***. The Examiner's reliance is misplaced. Neither recitation in ***Cham*** in any way suggests using modified versions of the ***Cham*** compounds as intermediates in solarmgine or solasonine synthesis. Indeed, ***Cham*** teaches away from the use of these compounds as intermediates. The ***Cham*** compounds are an end in themselves – for use in the control of cellular functions.

In her Advisory Action, the Examiner also argues that the other cited documents teach conventional synthesis and that such synthesis could be useful with the compounds of ***Cham*** to synthesize solunum glycosides. The Examiner is mistaken. The skilled worker would

have had no reason to use the end products of ***Cham*** in any synthetic method, much less the specific ones of the amended claims. Applicant requests reconsideration and withdrawal of this rejection.

CONCLUSION

Applicants request favorable consideration and early allowance of the amended claims.

Respectfully submitted,

James F. Haley, Jr. (Reg. No. 27,794)
Attorney for Applicants
c/o ROPES & GRAY LLP
Customer No. 1473
1211 Avenue of the Americas
New York, New York 10036
Phone: 212.596.9000
Fax: 212.596.9090